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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,267	03/23/2006	Qingshan Huang	H0757.70000US00	6419
23628 7590 11/18/2008 WOLF GREENFIELD & SACKS, P.C. 600 ATLANTIC AVENUE BOSTON, MA 02210-2206			EXAMINER TSAY, MARSHA M	
			ART UNIT 1656	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/526,267	Applicant(s) HUANG ET AL.	
	Examiner Marsha M. Tsay	Art Unit 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 August 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19-37 is/are pending in the application.
- 4a) Of the above claim(s) 30-35 and 37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19-29 and 36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>03.02.05; 03.23.06</u> | 6) <input type="checkbox"/> Other: _____ |

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Applicant's election with traverse of Group I, claims 19-29, 36, to SEQ ID NO: 46, in the reply filed on August 4, 2008 is acknowledged. The traversal is on the ground(s) that the instant application is a national stage application and that unity of invention is present. Applicants disagree with the Examiner's characterization of the special technical feature. Special technical features are "those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art." (see 37 CFR 1.475(a)). This is not found persuasive because the special technical features as defined in the restriction requirement is not shared by all the groups, i.e. the recombinant DNA in Group 2 is not shared by the remaining groups but is necessarily for the invention of Group 2. However, as noted in the restriction requirement, the restriction was made between product and process claims, and if the product of elected Group I is subsequently found allowable, the withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP 821.04. The reasons for the election of one specific SEQ ID NO. for examination are the same as noted in the restriction requirement.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-18 are canceled. Claims 30-35, 37 have been withdrawn from further consideration by the Examiner because they are drawn to non-elected claims. Claims 19-29, 36, to SEQ ID NO: 46, are currently under examination.

Priority: The request for priority to CHINA 02136766.3, filed September 2, 2002, is acknowledged.

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Claim Objections

Claim 20 is objected to because of the following informalities:

the use of the terms “peptide or protein” implies that the amino acids in a given sequence are linked by at least three consecutive peptide bonds, and should be identified by an appropriate sequence identifier (i.e. SEQ ID NO: 46). MPEP 4244.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-29, 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods and compositions of SEQ ID NO: 46 (a synthetic antimicrobial peptide) to treat an infectious disease induced by bacteria, fungi, and/or viruses, does not reasonably provide enablement for functional analogs or fragments or derivatives of SEQ ID NO: 46 that have antimicrobial activity and can treat an infectious disease induced by bacteria, fungi, and/or viruses. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art to ascertain which functional analogs, fragments and/or

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derivatives of SEQ ID NO: 46 function in the same way as the wild-type peptide. Thus there could be thousands of variants which contain substitutions, deletions, additions etc. Thus for the instant claimed invention, it would require an undue burden of experimentation for a skilled artisan to determine exactly which functional analogs or derivatives or fragments were active.

The factors to be considered in determining whether undue experimentation is required are summarized in *re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). The court in *Wands* states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In the instant case the quantity of experimentation would be large since there are myriad substitutions, deletions or insertions to choose from. The amount of guidance in the specification is minimal with regard to which amino acids in SEQ ID NO: 46 are essential for activity. No working examples are present of functional analogs or fragments or derivative SEQ ID NO: 46

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peptides. The nature of the invention is such that many different peptides that are substantially similar to SEQ ID NO: 4 may or may not have biological activity. The state of the prior art is that even proteins that are 99% similar to the wild-type peptide are at times not fully active. The relative level of skill in this art is very high. The predictability as to what substantially similar protein will have which activity is zero.

When the factors are considered in their entirety, the Wands analysis dictates a finding of undue experimentation and thus, the claim is not enabled.

Claims 19-29, 36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to SEQ ID NO: 46 or functional analogs or fragments and derivatives thereof, that have antimicrobial activity. *Vas-Cath Inc. V. Mahurkar*, 19USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” As stated above, SEQ ID NO: 46 or functional analogs or fragments and derivatives thereof, that have antimicrobial activity. However, the skilled artisan cannot necessarily envision the detailed structures of ALL of the functional analogs or derivatives and

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or fragments of SEQ ID NO: 46 that have the same functional activity as the wild-type SEQ ID NO: 46 because nowhere in the specification is it described which amino acids are even essential and critical for the wild-type protein to maintain its functionality, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the methods of making the claimed invention. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating or making it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Claims 19-20, 36 are rejected under 112 first paragraph because it refers to a peptide only by function. Even though Applicants have elected instant SEQ ID NO: 46 for examination, said sequence is not recited in base claim 19; therefore, the following rejection may apply.

The court of Appeals for the Federal Circuit has recently held that such a general definition does not meet the requirements of 35 U.S.C. 112, first paragraph. “A written description of an invention involving chemical genus, like a description of a chemical species, requires a precise definition, such as be structure, formula {or} chemical name, of the claimed subject matter sufficient to distinguish it from other materials.” *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). The court held that “in claims involving chemical materials, generic formulae usually indicate with specificity what generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed

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genus. In claims to genetic material, however, a generic statement such as “vertebrate insulin cDNA” or “mammalian insulin cDNA,” without more, is not an adequate written description of the genus because it does not distinguish it from others. One skilled in the art therefore cannot, as one can do with a fully described genus visualize the identity of the members of the genus”.

Here, the instant claims are reciting a peptide by what it does (i.e. antimicrobial activity), rather than by what it is (i.e. in terms of structure).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19-29, 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 recites functional analog. It is unclear what is meant by functional analog.

Claim 20 does not specify what the symbols A1, A2, A3, etc. can be, therefore it is unclear what the core structure is.

Claim 25 recites the N-terminal end of the core structure (A1-A2-A3-A4) is linked with a sequence having 11 amino acids. Claim 25 is dependent on claim 20, which recites the core structure (A1-A2-A3-A4)(A1'-A2'-A3'-A4'). It is unclear how a sequence having 11 amino acids can be linked to the N-terminal end of said core structure (A1-A2-A3-A4) since it appears said core structure is already linked to (A1'-A2'-A3'-A4').

Claim 26 recites wherein each of the amino acids 1, 3, 6 and 7 of the sequence is selected from the group consisting of Lys and Arg. Claim 26 is dependent on claim 25. It is unclear if

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the amino acids 1, 3, 6, and 7 are referring to the core structure (A1-A2-A3-A4)(A1'-A2'-A3'-A4')(A1''-A2''-A3''-A4'') or to the sequence having 11 amino acids. Further clarification is requested.

Similarly, it is unclear if in claim 27, the amino acid 2 of the sequence is referring to the core structure (A1-A2-A3-A4)(A1'-A2'-A3'-A4')(A1''-A2''-A3''-A4'') or to the sequence having 11 amino acids. Further clarification is requested.

Claim 28 recites the amino acids 4, 5, 8, 9, 10, and 11 of the sequence. Again, it is unclear if the sequence is referring to the core structure (A1-A2-A3-A4)(A1'-A2'-A3'-A4')(A1''-A2''-A3''-A4'') or to the sequence having 11 amino acids. Further clarification is requested.

Claims 21-24, 29, 36 are included in this rejection because they are dependent on the above claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 19-20, 21-25, 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Scott et al. (1999 Infection and Immunity 67(4): 2005-2009; IDS 03.23.06). As noted above, instant SEQ ID NO: 46 has been elected for examination. However, it is currently not recited in

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the instant claims; therefore the instant claims have been given its broadest and most reasonable interpretation, since the core structure has not been identified in claim 20, any peptide comprising an 8-mer and 12-mer is believed to be anticipatory art.

Scott et al. teach a series of synthetic antimicrobial peptides comprising a core structure of 2 sets of a 4-mer or 3 sets of a 4-mer (p. 2005 col. 2; claims 19-20). The synthetic antimicrobial peptides were designed and synthesized by Fmoc chemistry (p. 2005 col. 2; claim 29). In Table 1, Scott et al. teach the peptide CP α 2, a 30-mer having the sequence KWKKFIKKIGIGAVLKVLTTGLPALKLTKK, wherein the residues Gly, Val, and Leu are present at positions 10, 14, and 18 (claims 22-23, 25), and a Lys residue is present at positions 4 and 8 (claim 24). Further in Table 1, Scott et al. teach the peptide CP206, a 23-mer having the sequence KKWWKFIKKAVNSGTTGLQTLAS, wherein a Lys residue is present at positions 1, 5, 9 (claim 21).

Claims 19-20, 26-28 are rejected under 35 U.S.C. 102(e) as being anticipated by Hahm et al. (US 6800727). Hahm et al. teach SEQ ID NO: 1, a synthetic antimicrobial 20-mer comprising a core structure of 2 sets of a 4-mer or 3 sets of a 4-mer (col. 13; claims 19-20). The amino acids recited in claims 26-28 have been interpreted to be representative of residues from the core structure (A1-A2-A3-A4)(A1'-A2'-A3'-A4')(A1''-A2''-A3''-A4''). SEQ ID NO: 1 of Hahm et al. teaches Lys residues at positions 1, 3, 6, and 7 (claim 26), a Trp residue at position 2 (claim 27), and the residues Leu, Phe, Ile, Gly, Ile, and Gly at positions 4, 5, 8, 9, 10, 11 (claim 28).

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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Scott et al. (1999 Infection and Immunity 67(4): 2005-2009; IDS 03.23.06). The teachings of Scott et al. are outlined above. Scott et al. further disclose that said synthetic antimicrobial peptides can be used to treat bacteria growth in vitro and can be used in combination with antibiotics for treating LPS (p. 2005, 2008) but do not explicitly teach treating a subject having a bacterial infectious disease.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to administer the synthetic antimicrobial peptides of Scott et al. to a subject having a bacterial infection because Scott et al. teach that said synthetic antimicrobial peptides can be used to treat bacteria growth and used in combination with antibiotics (claim 36). Since antibiotics are known in the art to be administered to mammals for the treatment of bacterial infections, one of ordinary skill would be motivated to administer said antimicrobial peptides to a mammal for treatment of a bacterial infection since Scott et al. disclose that said antimicrobial peptide can successfully inhibit bacterial growth and can be used in combination with an antibiotic.

No claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is (571)272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Maryam Monshipouri/

Primary Examiner, Art Unit 1656

November 7, 2008